**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION**
**DECISION SUMMARY**
**ASSAY ONLY TEMPLATE**

**A. 510(k) Number:**
k042988

**B. Purpose for Submission:**
New product

**C. Measurand:**
Buprenorphine

**D. Type of Test:**
Qualitative lateral flow immunochromatographic test

**E. Applicant:**
Tianjin New Bay Bioresearch Company Limited

**F. Proprietary and Established Names:**
For Sure One Step Buprenorphine Test Card

**G. Regulatory Information:**

1. Regulation section:
   21 CFR §862.3650, Opiate Test System
2. Classification:
   Class II
3. Product code:
   DJG
4. Panel:
   Toxicology (91)

**H. Intended Use:**

1. Intended use(s):
   See Indications for Use below.
2. Indication(s) for use:
   "For Sure One Step Buprenorphine Test Card is an immunochromatographic immunoassay for qualitative determination of the presence of buprenorphine in human urine at cutoff concentration of 10 ng/ml. The assay provides a simple and rapid analytical screening procedure to detect buprenorphine in human urine.

   The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result. Gas chromatography /mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical and professional judgment should be applied to any drug of abuse test result, particularly when preliminary results are used."

3. Special conditions for use statement(s):
   The assay does not distinguish whether buprenorphine is being taken therapeutically or abused.

   This device is for prescription use only.

4. Special instrument requirements:
   None required. This is a hand-held, visually interpreted device.

**I. Device Description:**

The device consists of a porous membrane with areas containing bound antigen and colloidal gold labeled anti-buprenorphine mouse monoclonal antibodies in a plastic housing with a specimen well and a window to read the test results. A dropper is included with the Test Card, but a specimen collection container is not included. The test is packaged in a foil envelope.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):
   Microgenics CEDIA Buprenorphine Assay
   ACON OPI II One Step Opiate Test Strip
2. Predicate 510(k) number(s):
   k040316
   k040274
3. Comparison with predicate:
   The candidate device tests the same analyte as the CEDIA Buprenorphine Assay (k040316) and uses an antibody to detect the presence of the drug; however, cutoff concentration and the method of detecting the antibody-antigen complex are different.

   Both the candidate device and the ACON OPI II One Step Opiate Test Card use the same methodology, the same matrix, and time to result. Both are visually-read single use devices.

**K. Standard/Guidance Document Referenced (if applicable):**

None referenced.

**L. Test Principle:**

The devices employ lateral flow immunochromatographic technology and are based on the principle of competitive binding. Buprenorphine, if present in concentrations below the cutoff level, will not saturate the binding sites of antibody-coated particles in the device. The antibody-coated particles will then be captured by immobilized buprenorphine-specific conjugate and a magenta line will appear in the test line region. A line will not form if the sample contains drug in excess of the cutoff level because the drug will saturate all the binding sites of the drug-specific antibody. Each device contains a procedural control. Formation of a line in the control line region

indicates that the proper volume of urine has been added and membrane wicking has occurred. If a line does not form in the control region then the test is not valid and users are cautioned to repeat the test. A 'presumptive positive' is determined by the appearance of a procedural control line AND no line appearing next to the test region.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

*a. Precision/Reproducibility:*

Within-lot precision was established by testing drug-free human urine spiked with different concentrations of buprenorphine (n=15) as shown below:

**Within-Lot Precision: Rapid One Step Buprenorphine Test Card**

| Buprenorphine Concentration (ng/mL) | Expected Result | Correct Results |
|---|---|---|
| **0** | Negative | 15/15 |
| **5.0** | Negative | 15/15 |
| **7.5** | Negative | 13/15 |
| **10.0** | Positive | 15/15 |
| **12.5** | Positive | 15/15 |
| **15** | Positive | 15/15 |
| **25** | Positive | 15/15 |

Three lots were tested to establish inter-lot precision. Spiked drug-free human urine was tested 15 times at the concentrations shown below:

**Between-Lot Precision: Rapid One Step Buprenorphine Test Card**

| | | # Correct Results | | |
|---|---|---|---|---|
| **Buprenorphine Concentration (ng/mL)** | **Expected Result** | **Lot A** | **Lot B** | **Lot C** |
| **0** | Negative | 15/15 | 15/15 | 15/15 |
| **5.0** | Negative | 15/15 | 15/15 | 15/15 |
| **7.5** | Negative | 13/15 | 12/15 | 12/15 |
| **10.0** | Positive | 15/15 | 15/15 | 15/15 |
| **12.5** | Positive | 15/15 | 15/15 | 15/15 |
| **15** | Positive | 15/15 | 15/15 | 15/15 |
| **25** | Positive | 15/15 | 15/15 | 15/15 |

*b. Linearity/assay reportable range:*

Not applicable. This is a semi-quantitative device; a 'positive' result only suggests that buprenorphine is present in quantities above the cutoff level.

*c. Traceability, Stability, Expected values (controls, calibrators, or methods):*

This device has an internal process control. A magenta line appearing in the

control region confirms sufficient sample volume, adequate membrane wicking, and that the correct technique has been used. Users are informed not to interpret the test if a line does not form in the control region.

Control standards are not supplied with this device but the manufacturer recommends the use of commercially available controls. It is good laboratory practice to confirm the test procedure and to verify proper test performance. Users should follow all applicable guidelines for testing QC materials.

The sponsor claims the device is stable refrigerated or at room temperature for 18 months. The device should not be frozen.

*d. Detection limit:*

See the Precision/Reproducibility section above for performance around the stated cutoff concentration.

*e. Analytical specificity:*

Cross-reactivity of buprenorphine metabolites were determined by adding known amounts of metabolites to buprenorphine-free urine specimens. The following table lists the lowest concentration which yields a positive result for the compound. Cross-reactivity was calculated by dividing the concentration at which the compound yielded a positive result by the designated cut-off concentration.

**For Sure One Step Buprenorphine Card: Cross-reactivity of Compounds**

| Compound | Concentration (ng/mL) | Cross Reactivity (%) |
|---|---|---|
| Buprenorphine | 10 | 100 |
| Buprenorphine-3-B-D-glucuronide | 2.5 | 400 |
| Nalorphine | 1,000 | 1 |
| Norbuprenorphine | 30,000 | 0.03 |
| Norbuprenorphine-3-B-D-glucuronide | 30,000 | 0.03 |
| Codeine | 100,000 | 0.0001 |

Potential interference caused by other substances or drugs was evaluated by adding 100 ug/ml of each drug to buprenorphine-free urine and testing with the For Sure One Step Buprenorphine Card:

| Compounds that Do Not Cross React with the For Sure One Step Buprenorphine Card | | |
|---|---|---|
| Acetaminophen | Histamine | Oxycodone |
| Acetylsalicylic Acid | Hydromorphone | Phendimetrazine |
| Amikacin | Hydrochlorothiazide | Penicillin G |
| Amitriptyline | Imipramine | Pentobarbital |
| Ampicillin | Levorphanol | d-Propoxyphene |

| Compounds that Do Not Cross React with the For Sure One Step Buprenorphine Card | | |
|---|---|---|
| Arterenol | Ketoprofen | l-Propanol |
| Aspartame | D9-THC | Phencyclidine |
| Benzoic Acid | 11-Nor-D9-THC-9-COOH | Phenobarbital |
| Benzoylecgonine HCl | Methylphenidate | Phentermine |
| Caffeine | Methadone | Phenylpropanolamine |
| Chlorpheniramine | Methaqualone | l-Phenylephrine |
| Chlorpromazine HCl | Morphine | Quinine |
| Cimetidine | Morphine-3-glucuronide | Sodium Salicylate |
| Deoxyephedrine | 6-Monoacetylmorphine | Tryptophan |
| Dextromethorphan | Nalorphine | Tetracycline |
| Diazepam | Naloxone | Tetrahydrozoline |
| Diethylpropion | Naltrexone | Theophylline |
| 5,5 Dihydrocodeine | Noroxycodeine | Thioridazine |
| Doxylamine | Noroxymorphine | Trifluroperazine |
| Ecgonine HCl | Lansoprazole | *2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrroliodine (EDDP) |
| Ecgonine Methyl Ester | Oxazepam | |
| Heroin | Oxymorphine | |

Potential interference caused by endogenous and common compounds was assessed in drug-free and buprenorphine spiked urine (10 ng/mL). The expected results (negative and positive, respectively) were found with all compounds.

**Endogenous and Common Compounds that Do Not React with the For Sure One Step Buprenorphine Card**

| Substance tested | Conc. (mg/dl) | Substance tested | Conc. (mg/dl) |
|---|---|---|---|
| Acetone | 1000 | Urea | 2000 |
| Ascorbate | 300 | Ethanol | 1000 |
| Creatinine | 500 | DL-thyroxine | 12 |
| Globulin | 500 | Digoxin | 15 |
| Glucose | 1500 | Apomorphine | 10 |
| Hemoglobin | 300 | Tetracycline | 20 |
| NaCl | 6000 | D-glucuronic acid | 20 |
| Oxalic Acid | 50 | Uric Acid | 23 |
| Human serum albumin | 500 | Ampicillin (sodium) | 20 |

Aliquots of three negative urine samples of different specific gravity were spiked with a range of buprenorphine concentrations and the device was tested in duplicate with each parameter. The results demonstrate that specific gravity ranges from 1.003 to 1.030 did not affect the expected results or accuracy of the test.

The pH of an aliquoted negative urine pool was adjusted to a pH range of 5 to 9 in 1 pH unit increments; three of the four aliquots were spiked with buprenorphine. Final buprenorphine concentrations in the aliquots were between 0 and 20 ng/ml. The spiked, pH-adjusted urine was tested with the

Test Card in duplicate. The results demonstrate that varying ranges of pH do not interfere with the performance of the test.

*f. Assay cut-off:*
The stated cutoff of this assay is 10 ng/mL. Characterization of how the device performs analytically around the claimed cutoff concentration appears in the detection limit section, above. The Substance Abuse and Mental Health Services Administration (SAMHSA) has not recommended cutoff levels for buprenorphine tests.

2. Comparison studies:
   *a. Method comparison with predicate device:*
   Clinical samples (n=103) were collected at an outpatient facility in London, UK. An aliquot of each sample was intended pre-treated with glucuronidase, extracted using mixed-mode solid-phase technique, and then analyzed by GC/MS operating in full scan mode. Thus, all glucuronide metabolites in the original sample were converted to the parent compound. The urine aliquot used to test the device was not pre-treated with glucuronidase. A comparison of the two methods is shown below:

**Performance of For Sure One Step Buprenorphine Card Compared to GC/MS**

| | GC/MS Positive | GC/MS Negative | Total |
|---|---|---|---|
| **TNB Positive** | 34 | 15 | 49 |
| **TNB Negative** | 0 | 54 | 54 |
| **Total** | 34 | 69 | 103 |

Agreement between the methods was 85.4%. There are an unusually high number of false positives for this type of device. This could be due to the antibody's high cross-reactivity with buprenorphine glucuronide (400%: see *Analytical Specificity* section above) as many of the discrepant samples had buprenorphine present but at levels below the cutoff by GC/MS. Samples that were used to test the One Step device were **not** pre-treated with glucuronidase and therefore may have had metabolites present at sufficient levels to cross-react. The table below details the concentration of buprenorphine detected by GC/MS in the discrepant samples:

**For Sure One Step Buprenorphine Card:**
**Amount of Buprenorphine Present in Discrepant Samples**

| # | Test Card Result | BUP present (ng/mL) | # | Test Card Result | BUP present (ng/mL) | # | Test Card Result | BUP present (ng/mL) |
|---|---|---|---|---|---|---|---|---|
| 1 | Pos | 3 | 6 | Pos | 5 | 11 | Pos | 8 |
| 2 | Pos | 3 | 7 | Pos | 8 | 12 | Pos | 3 |
| 3 | Pos | 8 | 8 | Pos | 8 | 13 | Pos | 8 |
| 4 | Pos | 9 | 9 | Pos | 3 | 14 | Pos | 2 |
| 5 | Pos | 3 | 10 | Pos | 4 | 15 | Pos | 2 |

A sufficient number of clinical samples were around the cutoff as shown in the table below:

**Agreement between Buprenorphine Test Card and GC/MS (Cutoff 10 ng/mL)**

| | | Buprenorphine Conc. by GC/MS (ng/mL) | | | | |
|---|---|---|---|---|---|---|
| | | Negative | < -25% C/O | -25 % to C/O | C/O to +25% C/O | >25% C/O |
| | Conc. | 0 | <7.5 | 7.5 – 10 | 10 – 12.5 | >12.5 |
| Rapid One Step Buprenorphine Card | Pos | 0 | 9 | 6 | 1 | 32 |
| | Neg | 54 | 1 | 0 | 0 | 0 |

*b. Matrix comparison:*
Not applicable; this device is for use with urine only.

3. Clinical studies:
   *a. Clinical Sensitivity:*
   Not applicable. Clinical data is not typically provided in a 510(k) for this type of assay.
   *b. Clinical specificity:*
   Not applicable. Clinical data is not typically provided in a 510(k) for this type of assay.
   c. Other clinical supportive data (when a. and b. are not applicable):
   None provided.
4. Clinical cut-off:
   There are currently no SAMHSA recommendations for a clinical cutoff for buprenorphine.

5. Expected values/Reference range:
   Not applicable.

**N. Proposed Labeling:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**O. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.